UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,784	02/21/2007	Roger Francis Martin	Q96728	1165

23373 7590 07/12/2010

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER
JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
07/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

sughrue@sughrue.com
PPROCESSING@SUGHRUE.COM
USPTO@SUGHRUE.COM

Office Action Summary	Application No.	Applicant(s)	
	10/590,784	MARTIN ET AL.	
	Examiner	Art Unit	
	D L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/5/10 & 8/25/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-34* is/are pending in the application.

4a) Of the above claim(s) *23-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/5/10 & 8/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 8/25/06 wherein claims 1-18 were canceled and claims 19-34 were added.

Note: Claims 19-34 are pending.

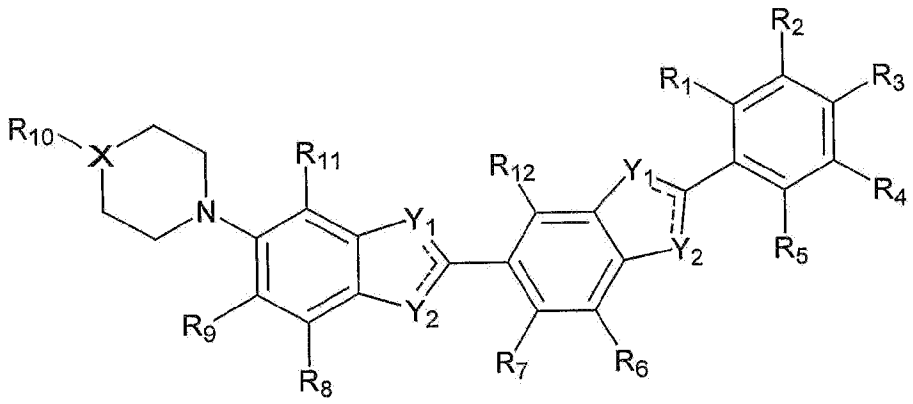
APPLICANT'S INVENTION

2. Applicant's invention is directed to cell targeting conjugates comprising a DNA ligand, radionuclide or photoactive moiety, and a target specific protein/peptide.

RESPONSE TO APPLICANT'S ELECTION

3. Applicant's election without traverse of Group I (claims 19-22) in the reply filed on 4/5/10 is acknowledged. Since the restriction requirement was not traverse, the restriction requirement is still deemed proper and is therefore made FINAL.

In addition, the Examiner acknowledges Applicant's election of the species on page 5 of the specification (Formula I) wherein an iodine-124 atom comprises the R10 group and constitutes an Auger electron emitting moiety; the compound of Formula I is conjugated to the somatostatin analogue, octreotide; and the conjugation is via an amide bond.



Formula (I)

Notes: Initially, Applicant's elected species was searched. However, since no prior art was found to reject the species, the search was expanded to the species (Hoechst) set forth in Harapanhalli et al (J. Med. Chem., 1996, Vol. 39, pp. 4804-4809). The search was not further expanded because prior art was found that could be used to reject the claims.

WITHDRAWN CLAIMS

4. Claims 23-34 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

112 FIRST PARAGRAPH REJECTIONS

Written Description Rejection

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 19-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is reminded that an Inventor is entitled to a patent to protect his work only if he/she produces or has possession of something truly new and novel. The invention being claimed must be sufficiently concrete so that it can be described for the world to appreciate the specific nature of the work that sets it apart from what was

before. The Inventor must be able to describe the item to be patented with such clarity that the Reader is assured that the Inventor actually has possession and knowledge of the unique composition that makes it worthy of patent protection. The instant application does not sufficiently describe the invention as it relates to the possible lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC10655, naturally occurring antibiotics, and analogs of lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine, CC10655, and naturally occurring antibiotics that are compatible with the instant invention. Likewise, the instant invention does not sufficiently describe the invention as it relates to all possible DNA minor groove binding ligands, and photoactive moieties that are compatible with the instant invention. While a generic claim may define the boundaries of a vast genus of chemical compounds, the question still remains whether the specification, including the originally filed claim language demonstrates that the Applicant invented species sufficient to support a claim to a genus. The problem is even more of a concern when claims use functional language to define the boundaries of a the claimed genus. For example, that a component in the conjugate is degradable within the target cells, is photoactive, is capable of being internalized by the target cells, or the group is a cellular uptake inhibition group. In such a case, the functional claim may simply claim a desired result, and may do so without describing species that achieve that result. However, what the specification must demonstrate is that Applicant has made a generic invention that achieves the claimed

result and do so by showing that Applicant has invented species sufficient to support a claim to the functionally defined genus. What the Reader gathers from the instant application is a desire/plan/first step for obtaining a desired result. Thus, while the Reader can certainly appreciate the desire for achieving a certain end result, establishing goals does not necessarily mean that an invention has been adequately described.

While compliance with the written description requirements must be determined on a case-by-case basis, the real issue here is simply whether an adequate description is necessary to practice an invention described only in terms of its function and/or based on a disclosure wherein a description of the components necessary in order for the invention to function are lacking. In order to satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the Inventor possessed the claimed invention at the time of filing. In other words, the specification should describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that the Inventor created what is the claimed. Thus, the written description requirement is lacking in the instant invention since the various terms as set forth above are not described in a manner to clearly allow persons of ordinary skill in the art to recognize that Applicant invented what is being claimed.

112 SECOND PARAGRAPH REJECTIONS

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-21: The claims as written are ambiguous because the claim appears to contain improper Markush terminology. Specifically, the claim appears to have a single DNA ligand and peptide/protein. However, the claim discloses that multiple radiomoieties may be present because of the phrase 'Auger electron emitting **and**/or gamma emitting **and**/or positron emitting atom or photomoiety' (see independent claim 19, lines 3-4). In addition, the claim as written appears to allow for multiple linkers because of the phrase 'hydrazone, **and**/or disulphide **and**/or amide bond' (see independent claim 19, line 6). Applicant is respectfully requested to refer to MPEP 803.02 for proper Markush terminology. Since claims 20 and 21 depend on independent claim 19, those claims are also vague and indefinite.

Claim 20: The claim as written is ambiguous because it is unclear what lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine analogues, CC10655, naturally occurring antibiotics, *and* analogs of lexitropsins, bibenzimidazoles, tribenzimidazoles, benzoxazoles, benzthiazoles, purines, DAPI, diarylamidines, SN series ligands, pentamidine, CC10655, and naturally occurring antibiotics Applicant is claiming that are compatible with the instant invention

Claim 21 contains trademark(s)/trade name(s). Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or

product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a cell target and, accordingly, the identification/description is indefinite.

Claim 22, lines 15-17: The claim is written are ambiguous because the claim appears to contain improper Markush terminology. Specifically, the claim discloses that R1 to R12 comprises an Auger electron emitting, gamma emitting moiety, a positron emitting atom ***and/or*** photomoiety' (see independent claim 19, lines 3-4).

Claim 22, lines 18-19: The claims as written are ambiguous because it is unclear what salts, pharmaceutically acceptable derivatives, prodrugs, and tautomers Applicant is referring to that are compatible and yield the desired results of a compound of Formula I.

103 REJECTIONS

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harapanhalli et al (J. Med. Chem., 1996, Vol. 39, pp. 4804-4809) in view of Mattes (US Patent No. 5,759,514).

Harapanhalli et al disclose the synthesis, DNA binding, and biodistribution of [125I/127I]iodoHoechst 33342 (see entire document, especially, page 4804, abstract; pages 4806-4807, bridging paragraph). Harapanhalli et al disclose that Hoechst 33528 (the parent structure of Hoechst 33342) has shown anti-tumor activity in vivo and

preclinical evaluations are occurring at the National Cancer Institute (page 4804, right column, first complete paragraph). The studies conducted by Harapanhalli et al indicated while [125I] labeled Hoechst 33528 may be used in vitro and in vivo, superior cellular uptake and DNA binding occurs using an analog, Hoechst 3342, of the parent structure. As a result, the analog was evaluated (page 4804, right column, first complete paragraph). In Scheme I (page 4805), iodoHoechst compounds are disclosed. The tumor targeting potential of [125I]iodoHoechst 33342 was evaluated. In view of the fact that the parent Hoechst 33528 is already undergoing clinical trial at the National Cancer Institute, it was suggested that a suitable carrier such as an antibody may be conjugated to the complexes (parent and analog) to ensure that it targets tumors effectively. While Harapanhalli et al suggest the possibility of attaching a carrier (i.e., antibody) to their radiolabeled Hoechst complex, the reference fails to specifically state that a carrier was attached and that the carrier could be a protein or peptide.

Mattes discloses a conjugate comprising a tumor cell targeting protein/peptide and a nucleic acid targeting small molecule labeled with an Auger electron emitting radionuclide. The tumor cell targeting protein or peptide may be an antibody or fragment thereof (see entire document, especially, abstract; column 1, lines 49-59; columns 1-2, bridging paragraph; column 2, lines 23-28). The nucleic acid binding or DNA intercalating small molecule may be labeled with one or more radionuclide such as 125I (column 2, lines 29-40). Many nucleic acid binding and DNA intercalating small molecules may be used. One possible molecule is Hoechst 3358 (column 2, lines 41-61, especially, line 60). Also, Mattes discloses that the results of their invention

demonstrate that an effective means of destroying the viability of tumor cells consist of administering to a patient a conjugate composed of a targeting protein (i.e., antibody) bound to a nucleic acid targeting small molecule derivatized with an Auger electron emitting radioisotope (column 7, lines 39-55; columns 7-8, bridging paragraph; column 8, claims 1-4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Harapanhalli et al using the teachings of Mattes and generate a cell targeting conjugate comprising a DNA ligand, an radionuclide, a peptide/protein target and a linker for the reasons set forth below. (1) Harapanhalli et al disclose that it is known in the art to label Hoechst 33258 with 125I. (2) Harapanhalli et al disclose that based on the fact that anti-tumor activity is known in the art for the parent structure of Hoechst (#33258), the tumor targeting potential of [125I]iodoHoechst 33342 was evaluated. (3) On page 4807 (left column, first incomplete paragraph), it is disclosed that if a the radiolabeled derivative of Hoechst can be conjugated with a suitable carrier such as an antibody, then it may be targeted to tumors effectively. In addition, on page 4807 (left column, first incomplete paragraph), it is disclosed that the parent Hoechst 33258 is already undergoing clinical trials. Thus, a skilled artisan would be motivated to generate a conjugate comprising a radiolabeled iodoHoechst compound (i.e., #33258 and 33342) conjugated to a carrier (i.e., antibody) as suggested by the prior art. (4) Mattes is cited because it discloses that it is well known in the art to generate a conjugate comprising a cell targeting protein/peptide, a nuclide acid targeting molecule, and an Auger electron emitting radionuclide. (5) In

addition, Mattes discloses that their DNA molecule may be Hoechst 33258 and may be labeled with 125I. Thus, it would have been obvious to a skilled practitioner in the art at the time the invention was made to generate a cell targeting conjugate comprising a DNA ligand and radionuclide (i.e., Auger emitting atom) linked to peptide/protein target as set forth in the instant invention. Since both Harapanhalli et al and Mattes disclose the radiolabeling of DNA ligands and both disclose the possibility of attaching a carrier to the radiolabeled complex, the references may be views as within the same field of endeavor. Thus, the reference teachings are combinable.

Notes: For Hoechst 33342 and 33528, the structures are encompassed by the instant invention when R10 = alkyl; R8 and R9 = hydrogen; Y2 = nitrogen; Y1 = NR' wherein R' = hydrogen; R6-R12 = hydrogen; R1-R3 = hydrogen; R4 = hydroxyl or OR group; R5 = halogen (iodine, specifically 125I or 127I); and one of R1-R12 comprise a peptide/protein.

PRIORITY DOCUMENT

13. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D L. Jones whose telephone number is (571)272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m.. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D L. Jones/
Primary Examiner
Art Unit 1618

July 6, 2010